Population of models of the electromechanical activity in human ventricular cells

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Population of cellular models is an approach allowing one to simulate experimental data with their natural variability. Model populations are built on a non-implausible parameter set calibrated on the ranges of observed experimental biomarkers. Populations of electrophysiological models of cardiomyocytes are widely used. Here we show that biomarkers of contractile activity are significant and should be accounted for to simulate normal (healthy) cardiomyocytes.

We used our model of the electromechanical activity of human ventricular cardiomyocytes (TP+M) [1] as a referent model to build a population of ventricular cardiomyocytes combining several approaches, History matching method included [2]. The model contains ten Tusscher-Panfilov-2006 description of human cardiac cell electrophysiology and our description of the cellular mechanical activity. To produce a population, we varied 13 input parameters in the TP+M model. Experimental biomarkers of action potential, calcium transient and force in human ventricular cardiomyocyte were used for model selection into the population (Fig. 1).

We showed that 1) model calibration on the only biomarkers of normal human action potential does not guarantee meeting normal biomarkers of calcium transient and force; 2) tests with varying mechanical conditions of cellular contraction reveal models with abnormal electrical activity that should be excluded from the population of normal human ventricular cardiomyocytes.

The TP+M population can be applied to assess pathological and pharmacological impacts on both electrophysiology and mechanical activity of cardiomyocytes.

1. Bazhutina ea, Prog Biophys Mol Biol. 2021. 159, 46-57.

2. Vernon ea. BMC Syst Biol. 2018. 12, 1.

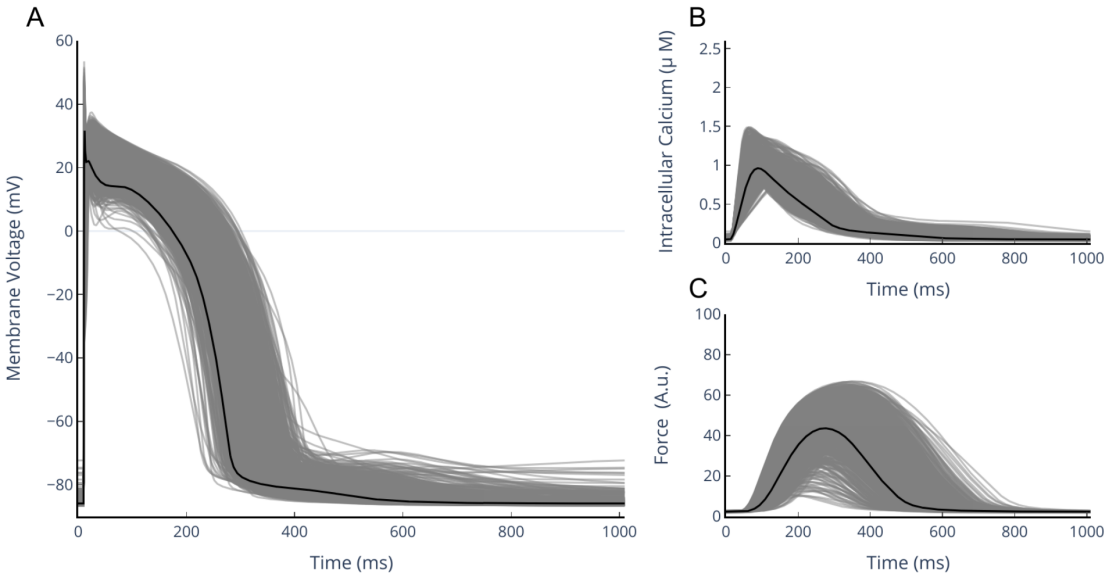

Figure 1 *Action potential (A), the intracellular calcium concentration (B), and the isometric force (C) in a TP+M population. Black lines are for the reference model*